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**Role of Biomarkers in Monitoring Gaucher
Disease and Potential of Biomarkers to Illuminate
Pathophysiologic Pathways**

A Thesis Submitted to the
Yale University School of Medicine
In Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

Hannah J. Yu
2008
New Haven, Connecticut

Role of Biomarkers in Monitoring Gaucher Disease and Potential of Biomarkers to Illuminate Pathophysiologic Pathways

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Objectives: 1.) Assess utility of biomarkers as a surrogate endpoint and a reflection of total body burden of Gaucher cells by examining correlations between biomarkers and liver volume and characterizing biomarker response to enzyme replacement therapy (ERT), and 2.) to gain insight into pathophysiologic pathways of GD.

Study Design: This is an observational study

Subjects and Methods: 114 patients with both pretreatment and post-treatment data were identified.

These patients were further subdivided into intact spleen and asplenic patients. Differences in means among the subgroups of patients were determined, then regression analyses were run to investigate correlations between biomarkers and liver volume. Multiple serial measurements of liver volume, spleen volume, and chitotriosidase while undergoing ERT were graphed in a subgroup of 5 patients.

Results: ACE, ferritin, transferrin saturation percentage, platelet count, and white blood cell count are all significantly increased in asplenic patients compared intact spleen patients. Correlations with liver volume and biomarkers were weak, but some were significant: In intact spleen patients, liver volume was positively correlated with chitotriosidase and ACE and negatively correlated with HDL, LDL, hemoglobin, and white blood cell count. In asplenic patients, liver volume was positively correlated with ACE and platelets. Chitotriosidase vs. liver volume and spleen volume responses to ERT showed a sigmoid curve.

Conclusion: This study shows that certain biomarker levels are increased in asplenic GD patients, suggesting that the spleen normally traps these substances in circulation. In addition, there were weak and inconsistent correlations between biomarkers and liver volume. These results in addition to the sigmoid shape of the relationship between spleen volume and liver volume with chitotriosidase levels indicate that chitotriosidase and perhaps other biomarkers are excreted from other organs as well.

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TABLE OF CONTENTS

| | |
|---|--------|
| Gaucher disease: Background----- | pg. 1 |
| Biomarkers of Gaucher disease----- | pg. 5 |
| Chitotriosidase----- | pg. 9 |
| CCL18----- | pg. 11 |
| Angiotensin-converting enzyme----- | pg. 12 |
| Tartrate resistant acid phosphatase----- | pg. 14 |
| Ferritin----- | pg. 15 |
| HDL and LDL cholesterol----- | pg. 16 |
| Triglycerides----- | pg. 17 |
| Immunoglobulins----- | pg. 17 |
| Aims----- | pg. 20 |
| Hypotheses----- | pg. 20 |
| Methods----- | pg. 20 |
| Patients----- | pg. 20 |
| Assays----- | pg. 21 |
| Statistics----- | pg. 22 |
| Results----- | pg. 23 |
| Biomarker values in patient subgroups----- | pg. 23 |
| Correlations between biomarker levels and normalized liver volumes in patient subgroups----- | pg. 26 |
| Effects of ERT on liver volume, spleen volume and chitotriosidase in individual patients----- | pg. 38 |
| Discussion----- | pg. 44 |
| References----- | pg. 49 |